

# Adaptimmune Reports Positive Results from its Pivotal SPEARHEAD-1 Trial in Patients with Synovial Sarcoma and MRCLS at CTOS

- SPEARHEAD-1 trial will meet its primary endpoint and data will be used to support BLA filing for afami-cel next year -
- The overall response rate (ORR) per Independent Review was 34% (36% in patients with synovial sarcoma and 25% for patients with MRCLS) and the disease control rate was 85% -
- As of the data cut-off, afami-cel has shown a favorable benefit:risk profile -
- Translational data confirm that afami-cel is active against MAGE-A4 expressing targets both *in vitro* and *in vivo*, and maintained high levels of persistence in the majority of patients followed for at least 6 months post-infusion -

PHILADELPHIA and OXFORDSHIRE, United Kingdom, Nov. 11, 2021 (GLOBE NEWSWIRE) -- Adaptimmune Therapeutics plc (Nasdaq:ADAP), a leader in cell therapy to treat cancer, will report updated clinical and translational data from its pivotal SPEARHEAD-1 trial with afamitresgene autoleucel (afami-cel, formerly ADP-A2M4) in patients with advanced synovial sarcoma or myxoid/round cell liposarcoma (MRCLS) at the Connective Tissue Oncology Society (CTOS) annual meeting.

“The positive results presented at CTOS further validate the potential of this therapy to address a great unmet medical need for patients with synovial sarcoma and MRCLS,” said Elliot Norry, Adaptimmune’s Chief Medical Officer. “We are confident that these data will support our BLA filing for afami-cel next year.”

“Afami-cel would provide a new treatment option for patients with synovial sarcoma, offering benefits that we have rarely seen with therapies currently available for this patient population,” said Dr. Brian A. Van Tine, Professor of Medicine and of Pediatrics at Washington University School of Medicine in St. Louis. “This is a game changer for patients with a high unmet medical need.”

Clinical data will be presented in an oral presentation by Dr. Brian Van Tine of the Washington University School of Medicine in St. Louis (Abstract #1080870) during the Immunotherapy & Immune Microenvironment Session starting at 10:00 a.m. EST on November 12<sup>th</sup>.

Preliminary translational insights from the Phase 2 SPEARHEAD-1 trial will also be presented in a poster (Abstract #1080366) by Dr. Sandra P. D’Angelo of Memorial Sloan Kettering Cancer Center during the Immunology & Immunotherapy Session beginning at

2:30 p.m. EST on November 12<sup>th</sup>.

### **Efficacy data validate the meaningful clinical benefit of afami-cel (data cut-off September 1, 2021)**

- 50 patients had received afami-cel (42 with synovial sarcoma, 8 with MRCLS)
  - Median age of patients was 41 years (range: 19 to 73) and they had received a median of three prior lines of therapy (range: 1 to 12)
  - The median dose was 8.5 billion transduced SPEAR T-cells (range: 2.7 to 10)
  - Three patients had scans awaiting Independent Review and 47 patients were evaluable
- The primary endpoint for SPEARHEAD-1 is response according to RECIST v1.1 evaluated by Independent Review<sup>1</sup>
- Based on the reported overall response rate, the trial will meet its primary endpoint in the final analysis planned later this year
  - Per Independent Review, the overall response rate was 34% (16/47 patients with partial responses [PRs])
  - The overall response rate was 36% in patients with synovial sarcoma, and 25% for patients with MRCLS
  - The disease control rate (defined as stable disease, PR, or CR) was 85% per Independent Review
  - The overall response rate and disease control rate per Independent Review were comparable to the assessments by Investigator Review (34% and 84%, respectively)
- Durability is encouraging and the median duration of response has not been reached
  - 75% of patients with response remain ongoing and the duration ranged from 4.3<sup>+</sup> to 65.3<sup>+</sup> weeks

### **Afami-cel was well-tolerated and has a favorable benefit:risk profile as of data cut-off**

- Thirty-three (66%) patients experienced adverse events of cytokine release syndrome (CRS), most of which were lower grade: Grade 1 or 2 (n=32); Grade 3 (n=1)
- The most common serious adverse event (SAE) of any grade was CRS reported in 6% of patients
- Eight (16%) patients experienced ≥ Grade 3 cytopenia at Week 4

### **Emerging translational data support clinical benefit seen in patients with afami-cel**

- Afami-cel SPEAR T-cells successfully engrafted in all patients and maintained high levels of persistence in most patients followed for at least 6 months post-infusion
- CD8<sup>+</sup> SPEAR T-cells in drug products administered killed >70% tumor cells *in vitro*
- Serum cytokine response profile indicates an IFN $\gamma$ -driven mechanism of action, signaling an afami-cel induced immune response
- Clinical benefit seen across a broad range of MAGE-A4 expression
- Post-infusion biopsies indicated that infiltrating afami-cel SPEAR T-cells co-localize with tumor and additional immune cells, with evidence of activated and proliferative state and adaptive-immune response

## Conclusion from the Phase 2 SPEARHEAD-1 trial

- The trial will meet its primary endpoint for efficacy for this pivotal trial
- As of September 1, 2021, overall response rate was 34% with a disease control rate of 85% per Independent Review in 47 heavily pre-treated patients
- Durability of responses is encouraging, and the median duration of response has not been reached
- The benefit:risk profile of afami-cel has been favorable, with mainly low-grade CRS and tolerable/reversible hematologic toxicities
- Translational data confirm that afami-cel is active against MAGE-A4 expressing targets both *in vitro* and *in vivo*
- These data will be used to support Adaptimmune's Biologics License Application (BLA) submission next year

## Overview of SPEARHEAD-1 trial design

SPEARHEAD-1 is a Phase 2, open-label trial for people with advanced synovial sarcoma or MRCLS to evaluate the efficacy, safety, and tolerability of afami-cel. Afami-cel SPEAR T-cells target MAGE-A4<sup>+</sup> tumors. MAGE-A4 is highly expressed in synovial sarcoma and MRCLS in the context of HLA-A\*02. Compelling clinical responses in patients with synovial sarcoma were previously reported with afami-cel in a Phase 1 trial (CTOS 2020).

Approximately 90 patients are planned to be treated: 45 in Cohort 1 and 45 in Cohort 2. Enrollment in Cohort 1 is complete, and Cohort 2 is currently recruiting. The primary efficacy analysis will be for Cohort 1 only, which will be used to support the BLA filing next year. No formal hypothesis testing is planned for Cohort 2. Cohort 2 will strengthen the efficacy and safety database and will aid in descriptive sub-group analyses.

Key eligibility criteria: ECOG performance status of 0 or 1; HLA\*02 positive with MAGE-A4 expression in  $\geq 30\%$  of tumor cells  $\geq 2^+$  by immunohistochemistry; aged  $\geq 16$  and  $\leq 75$  years; and patients must have received either an anthracycline- or ifosfamide-containing regimen. Eligible patients received afami-cel doses between  $1-10 \times 10^9$  transduced T-cells after receiving lymphodepleting chemotherapy.

## About Adaptimmune

Adaptimmune is a clinical-stage biopharmaceutical company focused on the development of novel cancer immunotherapy products for people with cancer. The Company's unique SPEAR (Specific Peptide Enhanced Affinity Receptor) T-cell platform enables the engineering of T-cells to target and destroy cancer across multiple solid tumors.

## Forward-Looking Statements

This release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 (PSLRA). These forward-looking statements involve certain risks and uncertainties. Such risks and uncertainties could cause our actual results to differ materially from those indicated by such forward-looking statements, and include, without limitation: the success, cost and timing of our product development activities and clinical trials and our ability to successfully advance our TCR therapeutic candidates through the regulatory and commercialization processes. For a further description of the risks and uncertainties that could cause our actual results to differ materially from those expressed in these forward-looking statements, as well as risks relating to our business in general, we

refer you to our Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on November 4, 2021, and our other SEC filings. The forward-looking statements contained in this press release speak only as of the date the statements were made and we do not undertake any obligation to update such forward-looking statements to reflect subsequent events or circumstances.

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<sup>1</sup> The primary endpoint will be evaluated using a one-sided exact-based Clopper-Pearson 97.5% confidence interval (CI). If the lower bound of the CI exceeds the response rate reported with historical second line therapy(ies) (18%), the trial will have met the pre-specified threshold for demonstrating efficacy.



Source: Adaptimmune Therapeutics plc